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Green and Blasecki Application 190 £09/\$06,430 Page 2

Attorney Do ANN 5046942-002330US Client Reference No.: 121

TECH CENTER 1600/2900

thereof

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where R' and R" is absent or a moiety independently selected from the group consisting of an amide, an imide, an ester, an anhydride, an ether, a methyl-alkyl ester, an ethyl-alkyl ester, an alkyl group, and an aryl group,

wherein R' can also represent an amide bond between the amine of said Glu and the side chain carboxylate of said Glu,

wherein R' is present if R" is present if R' is absent,

wherein the formula weight of said compound is less than about 5000 Daltons.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Reg. No. 47,413

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APPENDIX A

RSION WITH MARKINGS TO SHOW CHANGES

18. (Once Amended) A method of inhibiting neovascularization in a subject in need thereof comprising:

administering to said subject a pharmaceutical preparation comprising a pharmaceutically acceptable carrier and an amount of a compound effective to inhibit neovascularization with the formula of R'-Glu-Trp-R" or pharmaceutically acceptable salts thereof,

wherein R' and R" is absent or a moiety independently selected from the group consisting of an amide, an imide, an ester, an anhydride, an ether, a methyl-alkyl ester, an ethyl-alkyl ester, an alkyl group, and an aryl group,

wherein R' can also represent an amide bond between the amine of said Glu and the side chain carboxylate of said Glu,

wherein R' is present if R" is absent and R" is present if R' is absent, wherein the formula weight of said compound is less than about 5000 Daltons.

- 19. (As Filed) The method of claim 18, wherein the formula weight of said compound is less than about 1000 Daltons.
- 20. (As Filed) The method of claim 18, wherein said compound is selected from the group consisting of:

Ac-Glu-Trp, Suc-Glu-Trp, Cpr-Glu-Trp, But-Glu-Trp, and pyroGlu-Trp.

- 21. (As Filed) The method of claim 18, wherein said pharmaceutically acceptable salt is selected from the group consisting of sodium, potassium, ammonium, zinc, magnesium, and calcium.
- 22. (As Filed) The method of claim 18, wherein said pharmaceutically acceptable salt is selected from the group consisting of hydrochloride, hydrobromide, sulfate, bisulfate, acetate, oxalate, valarate, oleate, laurate, borate, benzoate, lactate, phosphate, tosulate, citrate, maleate, fumarate, succinate, and tartrate.
- 23. (As Filed) The method of claim 18, wherein the condition is hemangioma.

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Green and Blasecki Attorney Docket No.: 015542-002 Application No.: 09/506,430 Client Reference No.: 121 Page 4 (As Filed) The method of claim 18, wherein the condition is 24. vascularized malignant tumor or vascularized benign tumor. (As Filed) The method of claim 24, wherein the tumor is a tumor of the 25. meninges, an intracerebral tumor, a sarcoma, an osteosarcoma, a tumor of the esophagus, or a tumor of the trachea. (As Filed) The method of claim 24, wherein the tumor is a Lewis 26. carcinoma. (As Filed) The method of claim 24, wherein the tumor is Kaposi's 27. sarcoma. (As Filed) The method of claim 18, comprising administering to the 28. subject a dose of said compound of about 0.5 µg per 1 kilogram body weight to about 1 mg per 1 kg body weight. (As Filed) The method of claim 28, wherein the effective amount is 29. about 1 μg/kg to about 50 μg/kg body weight. (As Filed) The method of claim 28, wherein said dose is administered 30. daily over a period of 1 day to about 30 days. (As Filed) The method of claim 18, wherein said pharmaceutical 31. preparation is administered intramuscularly, intranasally, transdermally, or intrabronchially. (As Filed) The method of claim 18, wherein said pharmaceutical 32. preparation is administered intravenously, intraperitoneally, subcutaneously, or gastrointestinally. (As Filed) The method of claim 18, wherein said pharmaceutical

preparation is an injectable solution comprising 0.001% to 0.01% of said compound.

preparation is in a unit dose form comprising a tablet, a suppository, a capsule, an eye film,

(As Filed) The method of claim 18, wherein said pharmaceutical

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Green and Blasecki Application No.: 09/506,430 Attorney Docket No.: 015542-002 Client Reference No.: 121 Page 5 an inhalant, a mucosal spray, a nose drop, an eye drop, a toothpaste, an ointment, a watersoluble based cream, a solution, or a saline solution. (As Filed) The method of claim 34, wherein said unit dose form 35. consists essentially of 0.01 mg of said compound. (As Filed) The method of claim 18, further comprising administering 36. to the subject a vasoactive drug. (As Filed) The method of claim 36, wherein the vasoactive drug is an 37. angiotensin converting enzyme (ACE) inhibitor or a potassium channel opener (PCO). (As Filed) The method of claim 18, wherein the subject suffers from a 38. tumor and wherein the method further comprises administering a chemotherapeutic agent. (As Filed) The method of claim 18, wherein the subject is not immune 39. compromised. (As Filed) The method of claim 18, wherein the condition is 40. neovascularization in post-recovery cerebrovascular accident, neovascularization due to head trauma, restenosis following angioplasty, or neovascularization due to heat or cold trauma. (As Filed) The method of claim 18, wherein the condition is 41. neovascularization associated with substance-induced neovascularization of the liver, angiogenic dysfunction related to an excess of hormone, neovascular sequelae of diabetes,

neovascular sequelae to hypertension, or chronic liver infection.

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of diabetes is central serous chorioretinopathy.

(As Filed) The method of claim 41, wherein the neovascular sequelae

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APPENDIX B

PENDING CLAIMS SUBJECT TO EXAMINATION

18. (Once Amended) A method of inhibiting neovascularization in a subject in need thereof comprising:

administering to said subject a pharmaceutical preparation comprising a pharmaceutically acceptable carrier and an amount of a compound effective to inhibit neovascularization with the formula of R'-Glu-Trp-R" or pharmaceutically acceptable salts thereof,

wherein R' and R" is absent or a moiety independently selected from the group consisting of an amide, an imide, an ester, an anhydride, an ether, a methyl-alkyl ester, an ethyl-alkyl ester, an alkyl group, and an aryl group,

wherein R' can also represent an amide bond between the amine of said Glu and the side chain carboxylate of said Glu,

wherein R' is present if R" is absent and R" is present if R' is absent, wherein the formula weight of said compound is less than about 5000 Daltons.

- 19. (As Filed) The method of claim 18, wherein the formula weight of said compound is less than about 1000 Daltons.
- 20. (As Filed) The method of claim 18, wherein said compound is selected from the group consisting of:

Ac-Glu-Trp, Suc-Glu-Trp, Cpr-Glu-Trp, But-Glu-Trp, and pyroGlu-Trp.

- 21. (As Filed) The method of claim 18, wherein said pharmaceutically acceptable salt is selected from the group consisting of sodium, potassium, ammonium, zinc, magnesium, and calcium.
- 22. (As Filed) The method of claim 18, wherein said pharmaceutically acceptable salt is selected from the group consisting of hydrochloride, hydrobromide, sulfate, bisulfate, acetate, oxalate, valarate, oleate, laurate, borate, benzoate, lactate, phosphate, tosulate, citrate, maleate, fumarate, succinate, and tartrate.
- 23. (As Filed) The method of claim 18, wherein the condition is hemangioma.

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Green and Blasecki Attorney Docket No.: 015542-002 Application No.: 09/506,430 Client Reference No.: 121 Page 7 (As Filed) The method of claim 18, wherein the condition is 24. vascularized malignant tumor or vascularized benign tumor. (As Filed) The method of claim 24, wherein the tumor is a tumor of the 25. meninges, an intracerebral tumor, a sarcoma, an osteosarcoma, a tumor of the esophagus, or a tumor of the trachea. (As Filed) The method of claim 24, wherein the tumor is a Lewis 26. carcinoma. (As Filed) The method of claim 24, wherein the tumor is Kaposi's 27. sarcoma. (As Filed) The method of claim 18, comprising administering to the 28. subject a dose of said compound of about 0.5 µg per 1 kilogram body weight to about 1 mg per 1 kg body weight. (As Filed) The method of claim 28, wherein the effective amount is 29. about 1 μg/kg to about 50 μg/kg body weight. (As Filed) The method of claim 28, wherein said dose is administered 30. daily over a period of 1 day to about 30 days. (As Filed) The method of claim 18, wherein said pharmaceutical 31. preparation is administered intramuscularly, intranasally, transdermally, or intrabronchially. (As Filed) The method of claim 18, wherein said pharmaceutical 32. preparation is administered intravenously, intraperitoneally, subcutaneously, or gastrointestinally.

(As Filed) The method of claim 18, wherein said pharmaceutical

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preparation is an injectable solution comprising 0.001% to 0.01% of said compound.

preparation is in a unit dose form comprising a tablet, a suppository, a capsule, an eye film,

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Green and Blasecki Attorney Docket No.: 015542-0023 Application No.: 09/506,430 Client Reference No.: 121 Page 8 an inhalant, a mucosal spray, a nose drop, an eye drop, a toothpaste, an ointment, a watersoluble based cream, a solution, or a saline solution. (As Filed) The method of claim 34, wherein said unit dose form 35. consists essentially of 0.01 mg of said compound. (As Filed) The method of claim 18, further comprising administering 36. to the subject a vasoactive drug. (As Filed) The method of claim 36, wherein the vasoactive drug is an 37. angiotensin converting enzyme (ACE) inhibitor or a potassium channel opener (PCO). (As Filed) The method of claim 18, wherein the subject suffers from a 38. tumor and wherein the method further comprises administering a chemotherapeutic agent. (As Filed) The method of claim 18, wherein the subject is not immune 39. compromised. (As Filed) The method of claim 18, wherein the condition is 40. neovascularization in post-recovery cerebrovascular accident, neovascularization due to head trauma, restenosis following angioplasty, or neovascularization due to heat or cold trauma.

(As Filed) The method of claim 18, wherein the condition is

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neovascular sequelae to hypertension, or chronic liver infection.

angiogenic dysfunction related to an excess of hormone, neovascular sequelae of diabetes,

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